Atty, Dkt. No. EPI3007D (formerly TSRI 184.2C3)

REMARKS

Claims 21, 24-40, 43, 50, 54-63, 69-80, 101 and 102 are pending in this application.

Claim 21 is directed to plants that contain plant cells that express a non-plant biologically functional multimeric protein resulting from assembly of at least two different polypeptides. According to the method, the plant cells contain nucleic acid encoding the two different polypeptides each including a leader sequence which forms a secretion signal for individual polypeptide. As discovered by the inventors, proper processing of the each polypeptide is required so that the two polypeptides can form a biologically functional multimeric protein.

Claim 43 is directed to a plant cell containing nucleic sequence encoding an antigen-specific and containing the antigen specific immunoglobulin. In claim 43, the antigen-specific immunoglobulin is encoded by a heavy and light chain polypeptide.

Claim 21, 26 and 63 have been amended. The amendments have been made to clarify the invention that Applicants wish to pursue and raise no issue of new matter.

Claim 63 has been amended to replace "derived" with "obtained." Applicants submit that the amendment of does not limit the claim scope and that the terms "derived" and "obtained" have similar meaning and scope in the context of the claim.

New claims 103-106 have been added. Thus, the new claims are fully supported by the application and raise no issue of new matter. Support for claim 102 is found in the application at page 12-14. Support in claim 103 for "two or four different polypeptides" is found in the application at page 10, lines 12-13 (definition of multimeric protein) and at page 35, lines 5-12 (discussing secretory IgA).

REQUEST TO CORRECT INVENTORSHIP

Applicants again reiterate their request for a decision on the earlier filed request to correct inventorship under 37 C.F.R. § 1.48(b). The Request was filed along with the Request for Continued Prosecution Examination (CPA) on February 28, 2002. A copy of

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the CPA transmittal as filed requesting the inventorship change is attached herewith. An indication whether or not inventorship has been amended is earnestly solicited.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (Written Description)

The rejection of claims 21, 24-27, 29, 30, 39, 40, 78, 80 and 101 as being allegedly failing to comply with the written description requirement is respectfully submitted to be in error for the following reasons.

Applicable legal standard

The proper standard for determining compliance with the written description requirement of 35 U.S.C. § 112, first paragraph, is whether the specification reasonably conveys to the skilled artisan that the inventor was in possession of the claimed invention as of the filing date. See MPEP § 2163.02 (citing Ralston Purina Co. v. Far-Mar-Co., Inc., 227 USPQ 177, 179 (Fed. Cir. 1985)). The subject matter of the claimed invention need not be described literally in the specification in order to satisfy the requirements of 35 U.S.C. § 112, first paragraph. Id. In a careful analysis of the written description requirement provided by the Patent and Trademark Office in its Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶1, "Written Description" Requirement, it is stated that an adequate written description "may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the Inventor had possession of the claimed invention." 66 Fed. Reg. 1099, 1105 (2001) (emphasis added).

The specification provides adequate written description for claims 21, 24-27, 29, 30, 39, 40, 78, 80 and 101.

The Examiner has rejected all claims that relate to plant cells with nucleic acid encoding biologically functional multimeric protein comprising at least two different polypeptides. Although the Examiner appears to admit that the specification provides

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adequate written description for plant cells expressing antibodies, it is concluded that this does not constitute a substantial portion of the genus of cells expressing different multimeric proteins.

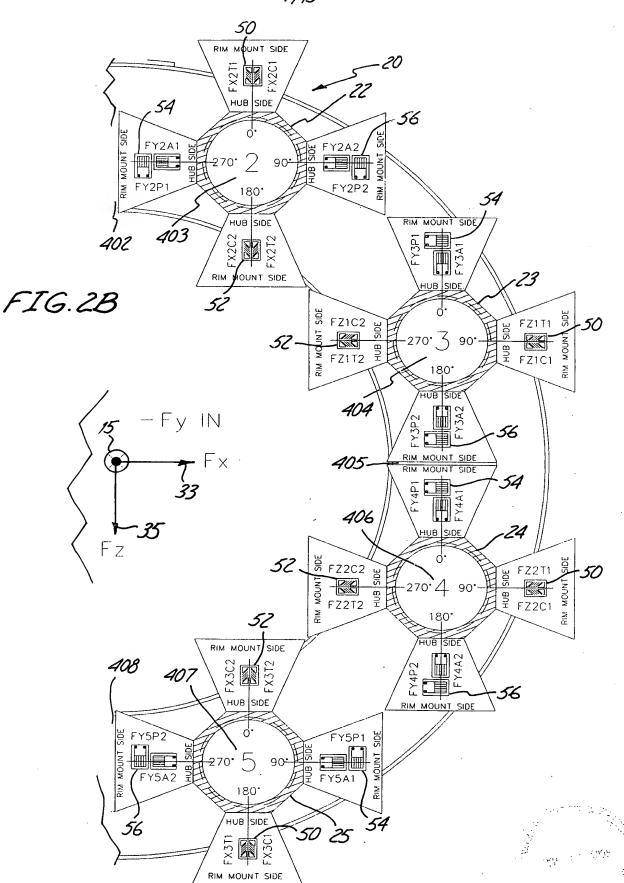
It is respectfully submitted that this conclusion is in error. First, Applicants point out that the inventors' original success with expressing the 6D4 IgG class catalytic antibody in plants led directly to the successful expression in plants of a complete IgA secretory immunoglobulin. Secretary IgA is a complex multisubunit protein, requiring the assembly of ten subunits representing four different polypeptides. Secretory IgA is a dimeric molecule, the monomers stabilized by a J chain and a secretory component.

Example 15 of the patent application at pages 90-102 describes the process used for expressing secretory IgA in plants. An IgA like heavy chain was formed from the V_Hγ, C_Hγ1 and C_Hγ2 domains of the Guy 13 antibody heavy chain and Cα2 and Cα3 domains of the MOPC 315 IgA myeloma heavy chain. *Id.* at Page 91. A plant cell was then prepared containing nucleic acid encoding the hybrid heavy chain, the Guy 13 kappa light chain, a mouse J (Joining) chain (Page 96) and a mouse secretory component (page 96). Ten transgenic plants were produced in which all expressed a fully assembled secretory IgA molecule of 470Kd. *Id.* at page 98. Proper assembly of plant produced secretory IgA was demonstrated by the molecular weight and by binding activity curves which showed similar results to native antibody from hybridoma cells. *Id.* at page 99.

Notably, assembly of the multimeric secretory IgA was very efficient, involving more than half of the total antibody. *Id.* at page 100. Furthermore, this was achieved by using an identical expression system for each subunit; i.e., the same leader sequence and promoter (36S transcript of cauliflower mosaic virus) were used.

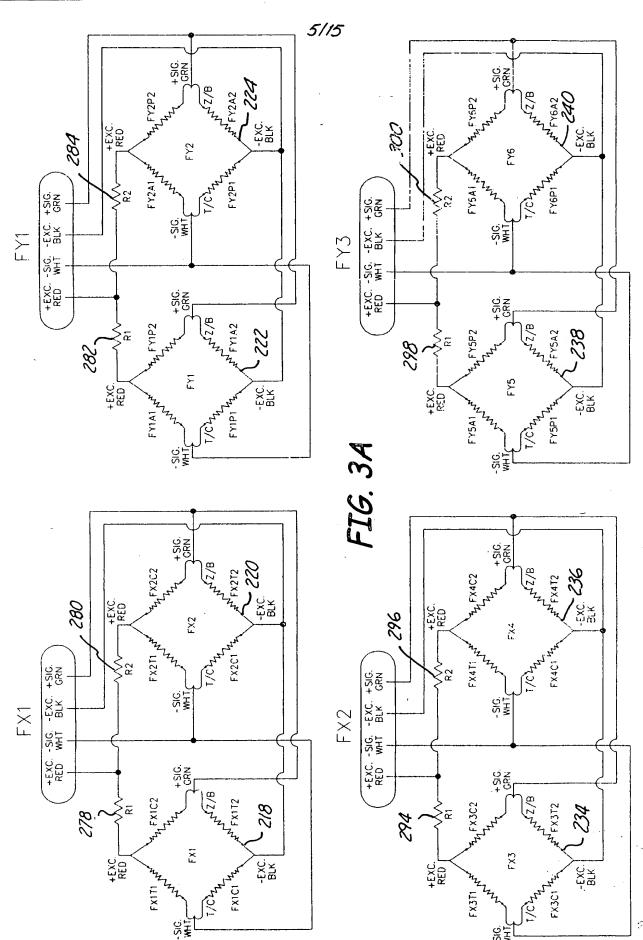
Thus, it is respectfully submitted that one skilled in the art would acknowledge that the application provides substantial evidence supporting the ability of plant cells to assemble complex multimeric proteins. In addition, nucleotide sequence encoding a wide array of multimeric proteins is readily available in public repositories and the skill in the art

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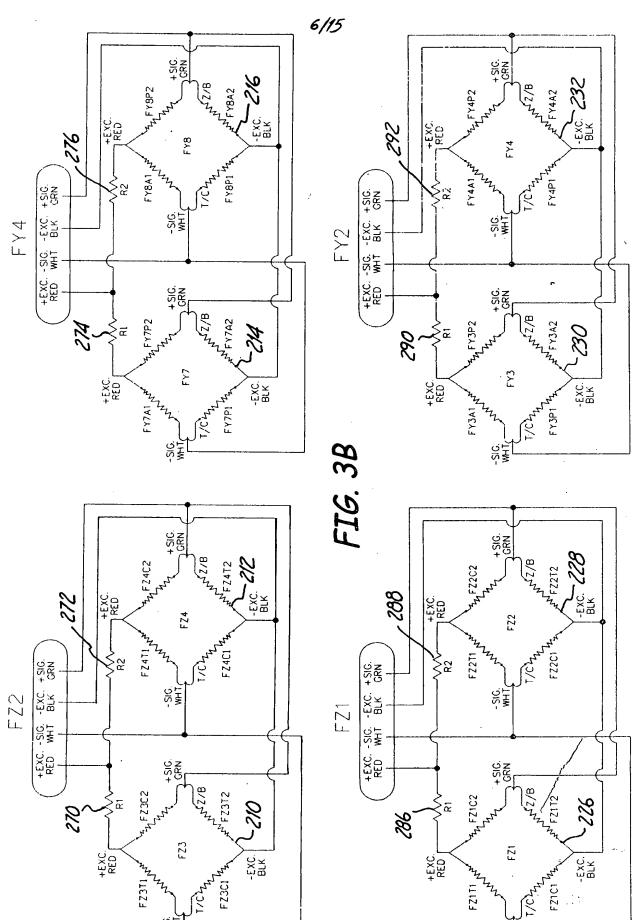


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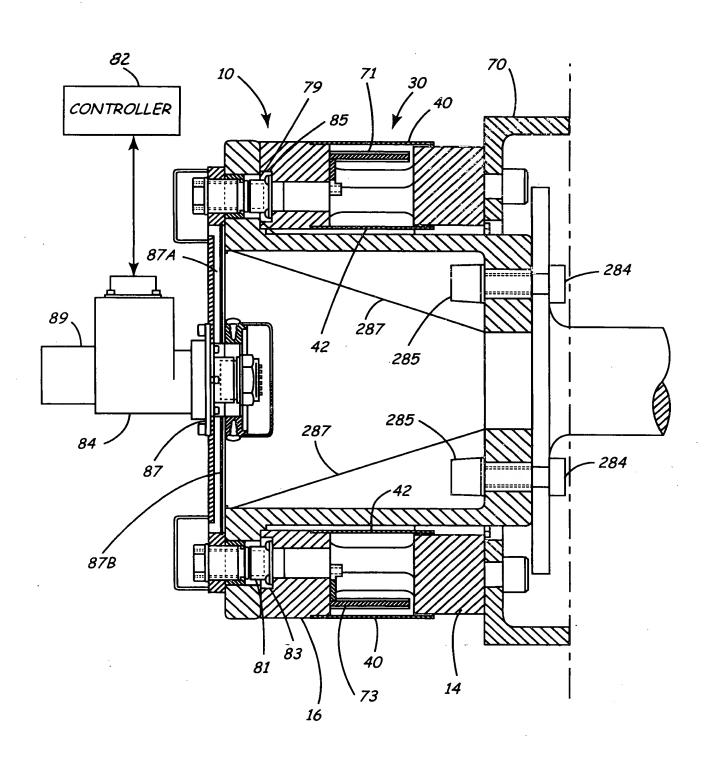
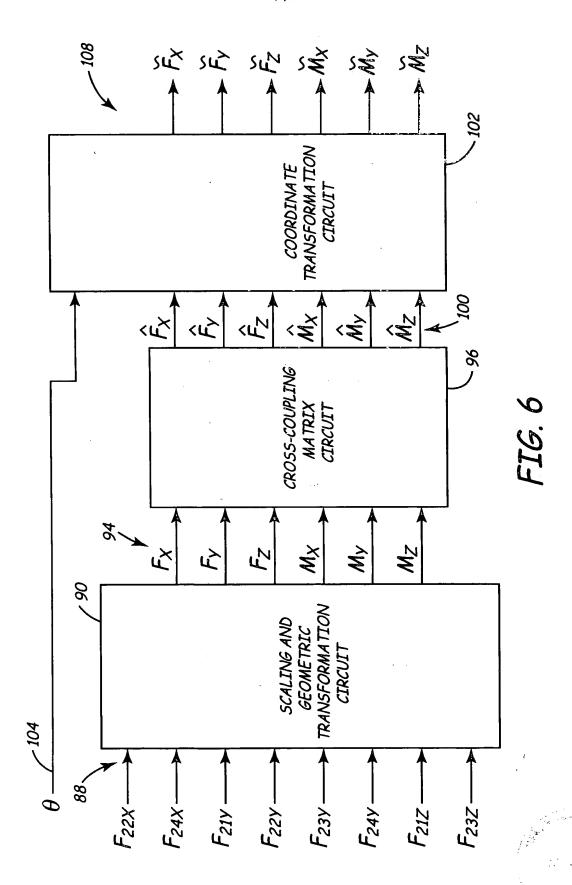
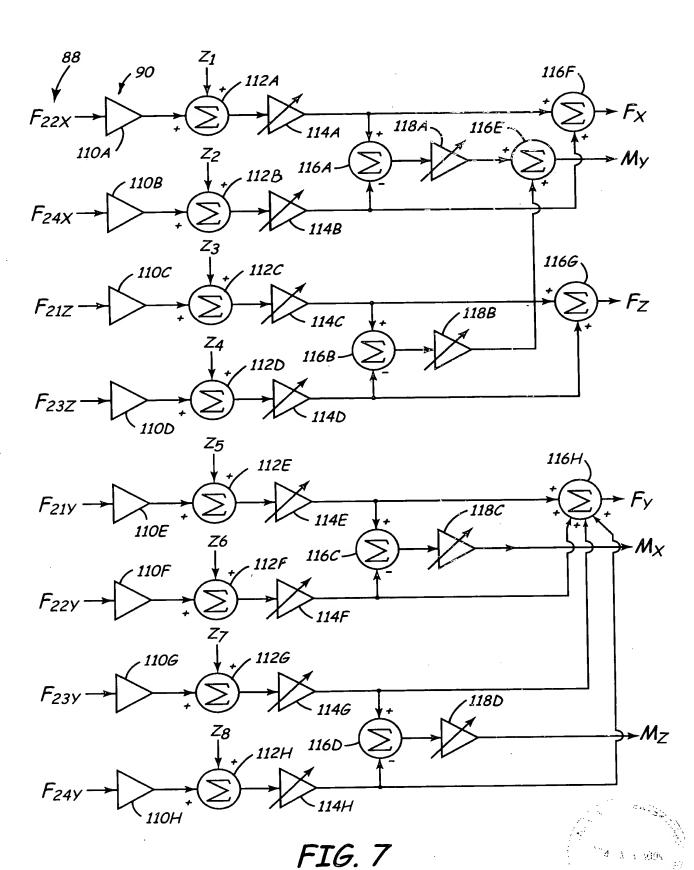


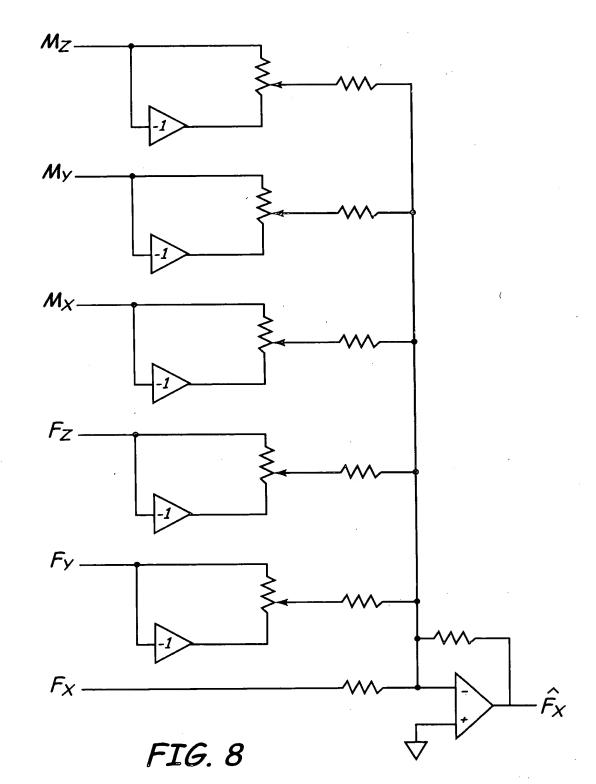
FIG. 5



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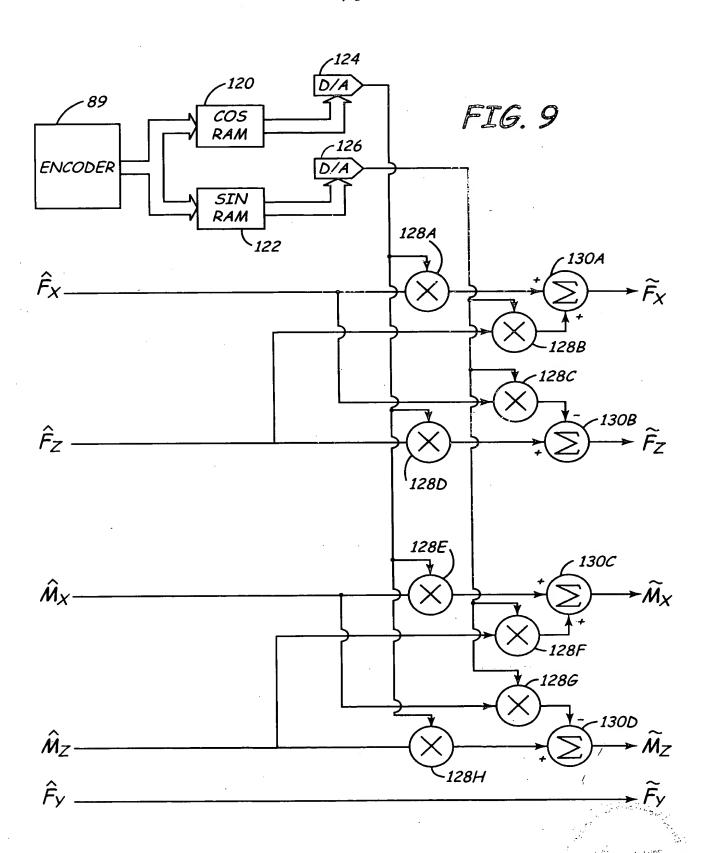






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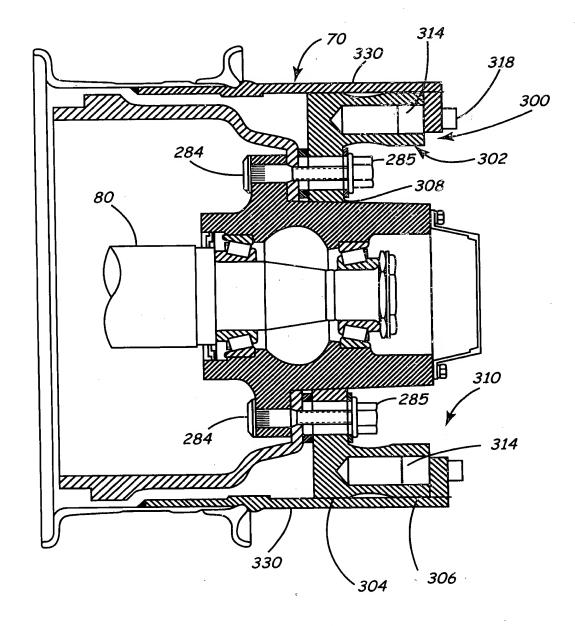


FIG. 10A